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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,974	01/27/2000	Connie S. Schmaljohn	003/115/SAP RIID96-10	9304

7590 11/04/2002

Attn MCMR JA Elizabeth Arwine Patent Atty
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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/04/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/491,974	Schmaljohn et al.
Examiner	**Art Unit**
Joseph T. Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 21, 2002*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *28-51* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) ☒ Claim(s) *46 and 47* is/are allowed.

6) ☒ Claim(s) *28-32, 35-41, 44, 45, 48, and 49* is/are rejected.

7) ☒ Claim(s) *33, 34, 42, 43, 50, and 51* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application filed January 27, 2000, claims benefit of provisional application 60/117,680, filed January 29, 1999.

Applicants' amendment filed August 21, 2002, paper number 17, has been received and entered. Claims 28-51 are pending and currently under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-32, 35-42, 44, 45 and 49 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schmaljohn (Rev. Med. Virol., 4:185-196, 1994), Chu *et al.* (J. Virol., 69(10):6417-6423, 10/95), Montgomery *et al.* (Pharmacol. Ther., 74(2):195-205, 1997), Donnelly *et al.* (Ann. Rev. Immunol., 15:617-648, 1997), and Arikawa *et al.* (Virol., 176:114-125, 1990).

Applicants summarize the basis of the rejection and argue that given the specific teachings of each of the references one would not have been motivated to combine the cited references nor would have had an expectation of success that the resulting composition resulted

in an effective vaccine. More specifically, Applicants argue that Schmaljohn and Chu *et al.* teach recombinant vaccinia virus vaccines not DNA vaccines, and that Arikawa *et al.* only mentions the use as a vaccine. Further, it is argued that differences between a vaccinia virus and a DNA vaccine would not allow one to predict whether the DNA vaccine will work, pointing to the fact that (1) a vaccinia virus elicits an immune response itself and that (2) RNA viruses, like the Hantaan virus instantly claimed, may contain sequences which in the context of a vector other than vaccinia would be rendered inoperable. Applicants argue the differences between vaccinia and DNA vaccine would not lead one to use the methods disclosed in Montgomery *et al.* and Donnelly *et al.* Finally, it is argued that Arikawa's motivation to design "recombinant DNA vaccines" fails to provide the necessary guidance to achieve a vaccine and fails to provide for the deficiencies of Schmaljohn and Chu *et al.* See Applicants' amendment, pages 1-4. Applicants' arguments have been fully considered, but not found persuasive.

First, it is noted that claim 28 is not directed to a vaccine *per se*, rather it is directed to a composition. The effectiveness of the composition as a vaccine is not a necessary requirement with respect to the composition. However, with respect to claim 48, Examiner would agree that the resulting polynucleotide must encode an antigen which confers a protective immunity to the Seoul, Dobrava or Hantann virus. Further, for both the composition and the method of use, the claims are broadly drawn to any polynucleotide operative in a mammalian cell and does not exclude the use of any particular vector as long as it is functional in a mammalian cell. With respect to Applicants' arguments regarding the difference between a vaccinia virus and a DNA

vaccine, Examiner would note the present claims encompass attaching the RNA from a vaccinia virus to the particle. It appears that agree that Applicant's arguments are directed against the references individually, however one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, clearly the hantaan virus proteins encoded by the M, G1 and G2 genes were known and demonstrated to serve as effective antigens in a vaccine composition as demonstrated by Schmaljohn, Chu *et al.* and proposed by Arikawa *et al.* Further, the antigens can be generated and provided by a variety of polynucleotide vectors. Clearly, the art teaches that there is an expectation that these particular hantavirus proteins would serve as antigens in a vaccine. In response to applicant's argument that vaccinia vectors and plasmid vectors differ significantly and represent nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, as set forth in the previous office action, Montgomery *et al.* reviews the state of the DNA vaccine art and teaches that "[i]f known antigens elicit protective antibodies from a natural infection, results in many disease models support the hypothesis that expression of the antigen from a plasmid will elicit a similar response" (page 198, left column). To the same extent, Donnelly *et al.* reviews the state of the DNA vaccine art and teaches DNA vaccines offer

a simple alternative to other methods involving e.g. live attenuated vaccinia virus recombinants which "may be restricted in use due to concerns about their safety" (page 619). Donnelly further draw attention to the "remarkable number of publications demonstrating efficacy of DNA vaccines in various preclinical models that have appeared since the publication of the initial demonstration of the generation of protective efficacy attest to the simplicity as well as the robustness of the technology" (page 620) and discusses the advantage and simplicity associated with being able to alter constructs or mixing different plasmid to explore the use of different forms of an antigen (see for example page. 625). It is noted that Applicants do not argue that the each of the specific embodiments instantly claimed are not set forth, rather that the references would not be combined with any expectation of success. However, each of the cited references are within the art of vaccines. One of skill in the art would be apprised of the various means to make and use a vaccine composition. Clearly, Schmaljohn, Chu *et al.* and Arikawa *et al.* provide evidence and motivation for a vaccine comprising the hantavirus proteins encompassed by the claims. Further, in the art of vaccines, DNA vaccines were generally known and demonstrated to be effective for known antigens. As set forth previously, given the differences between a vaccinia virus vaccine and DNA vaccine one of ordinary skill in the art would have been further motivated to combine these teachings in view of the advantages of DNA vaccines over live vaccinia virus vaccines since DNA vaccines are predicted to be safer, easier to maintain, less expensive, and offering greater flexibility, including protection against multiple antigens and/or pathogens as specifically suggested by Donnelly and Montgomery *et al.* Finally, it should be

noted that the courts support that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (CAFC 1988). In the instant case, the antigens encompassed by the instant claims were known, used and shown to be effective in vaccine compositions and in light of the teachings of Montgomery and Donnelly, there would have been a reasonable expectation of success to formulate these antigens in the form of a DNA vaccine.

Thus, for the reasons above and of record, the claimed invention as a whole was clearly *prima facie* obvious, and therefore the rejection is maintained.

Conclusion

As noted in the previous office action, claim 46 and 47 are allowed. Claims 33, 34, 42, 43, 50 and 51 are objected to because they depend on rejected claims, however would be found allowable if rewritten in independent form encompassing all the limitations of the independent claim and any intervening claims. Specifically, the claims directed to SEQ ID NO: 1 and the specific construct set forth in SEQ ID NO: 3 are free of the art of record because the antigenic determinants comprised by these specific sequences have not been previously disclosed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Deborah Crouch

Joseph T. Woitach

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630